Chapter 4
Metyrapone Stimulation Test

Indication: To evaluate HPA axis integrity. It is a sensitive alternative test to insulin tolerance test (ITT) in order to evaluate the adrenocorticotrophic hormone (ACTH) reserve.

Preparation: The patient may eat and drink normally prior to the test.

Materials Needed:

ACTH:
Lavender top tube on ice

Transport Temperature:
Frozen;

Note: Separate plasma from cells ASAP

Cortisol and 11 deoxycortiol (DOC):
Gold top tube

Metyrapone po (30 mg/kg body weight, or 2 g for < 70 kg, 2.5 g for 70 to 90 kg, and 3 g for > 90 kg)

Assay for Cortisol and ACTH: Chemiluminescence Assay (CLIA).

Assay for 11 DOC: LC-MS/MS.

Precautions: Hypotension, nausea, vomiting, abdominal discomfort or cramping, and musculoskeletal pain in patients with adrenal insufficiency may happen. Metyrapone can also cause dizziness, sedation, and allergic rash.

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Interpretation:

Metyrapone blocks the conversion of 11-deoxycortisol to cortisol by CYP11B1 (11-beta-hydroxylase, P-450c11), the last step in the synthesis of cortisol, and induces a rapid fall of cortisol and stimulation of ACTH.

1. A normal response to the overnight single-dose test consists of [1–3]:
   - A serum cortisol concentration at 8 AM of less than 5 μg/dL (138 nmol/L) confirms adequate metyrapone blockade.
   - An 8 AM serum 11-DOC concentration >7 mcg/dL (>200 nmol/L).

2. A lack of achieving a serum 11-DOC concentration >7 mcg/dL in the presence of a serum cortisol >5 mcg/dL may be related to a lack of adequate 11 beta hydroxylase blockage. In such patients, the test needs to be repeated after taking higher dosage of metyrapone.

Caveats:

- The metyrapone test is the most sensitive method to detect partial defects in pituitary ACTH secretion [1, 3].
- Cortisol levels measured by conventional immunoassays can be falsely elevated by the interference of increased 11-deoxycortisol levels induced by metyrapone; Liquid chromatography tandem mass spectrometry steroid assays give the best results [4].
- Similar to ITT, the metyrapone test is not indicated for evaluation of patients suspected to have primary adrenal insufficiency. In such cases, measurement of morning serum cortisol, plasma ACTH level, or ACTH stimulation would be preferred.

Procedure: Completed as outpatient

1. Patient ingests metyrapone (30 mg/kg body weight, or 2 g for <70 kg, 2.5 g for 70–90 kg, and 3 g for >90 kg body weight at midnight/bedtime with a glass of milk or a small snack.
2. Serum 11-deoxycortisol, cortisol, and plasma ACTH are measured between 7:30 and 9:30 AM the next morning [1, 2].

References

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